Women and Ischemia Syndrome Evaluation (WISE)
Diagnosis and Pathophysiology of Ischemic Heart Disease
Workshop

October 2-4, 2002

Session 4

1. Topic and Author

Estrogen plus Progestin Trial Results
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2. Where we stand in 2002. Overview/rationale for inclusion of topic.

WHI Estrogen + Progestin trial randomized 16608 postmenopausal women with intact uteri to conjugated equine estrogens (0.625 mg) with medroxyprogesterone acetate (2.5 mg) daily or identical-appearing placebo. The trial intervention was halted in July, 2002, following recommendation of the Data Safety Monitoring Board due to an excess of invasive breast cancer among woman assigned to combined Estrogen + Progestin (HR 1.26, 95% CI 1.00 – 1.59). The pre-specified primary outcome was a composite of non-fatal myocardial infarction and coronary death. Among women assigned to active Estrogen + Progestin, an increased risk of MI/CHD death (HR 1.29, 95% CI 1.02-1.63) was observed. This risk was particularly prominent in the first year of treatment, and was similar among women with (~3% of the cohort) or without prior CHD or prior hormone use. Though younger women had lower absolute risk for MI/CHD death, increases in relative risks in the E+P group were similar across the age ranges of 50-59, 60-69, and 70-79. Coronary revascularization rates were similar in the placebo and active treatment groups. Incident stroke was also more frequent among women assigned to active Estrogen + Progestin (HR 1.41, 95% CI 1.07-1.85).

The WHI Estrogen alone trial, which randomized 10,739 women with prior hysterectomy to conjugated estrogens or placebo, is ongoing.

3. Current challenges and the most important issues for future research

Identification of women at highest risk for coronary events during the first years on HRT
Role of SERMS, other estrogen formulations

4. Current challenges in the areas of communicating messages to health care community, patients and the public

How to communicate “bad news” to the participants, the public, and the profession, and how to best offer alternatives

5. Translating new findings to improved diagnosis and treatment/saving lives.

Acceptance of the findings has varied by specialty. There has been wide but not universal acceptance of the major finding, that E+P does not prevent MI/CHD death and may increase risk. ACOG and the manufacturer has accepted that use should mainly be for the short term treatment of menopausal symptoms, but individual gynecologists continue to question the findings. Women need to be informed about alternatives for preventing heart disease, osteoporosis, and management of menopausal symptoms. Continuing education to the profession and the public will be needed.

6. **References.**

JAMA 2002;288:321-33